Endogenous Opiate Alkaloids and Human Skin

To the Editor:

Endogenous morphine and codeine have been identified in the central nervous system and a variety of peripheral tissues (e.g., heart, adrenal, and skin) (Donnerer *et al*, 1987). Mammalian tissues not only contain morphine and codeine, but also synthesize these opiate alkaloids (Donnerer *et al*, 1986; Weitz *et al*, 1987). Studies also indicate a physiologic role in mammals for these agents as drugs and experimental manipulations (e.g., fasting) can alter the levels of morphine and codeine (Horak *et al*, 1993; Lee and Spector, 1991). In terms of ligand affinity, morphine is the prototypic agonist for the μ-opiate receptor (Pasternak, 1993).

It is in this context we read with great interest the paper entitled "Expression of μ-Opiate Receptor in Human Epidermis and Keratinocytes" in the *Journal of Investigative Dermatology* (Bigliardi *et al*, 1998). When the investigators examined the role of the epidermal keratinocyte in the interface of neurologic, immune, and dermatologic systems, they cited evidence for the production of proopiomelanocortin (POMC) by human epidermal keratinocytes (Schauer *et al*, 1994). A derivative of POMC is β-endorphin. They hypothesized that given the presence of β-endorphin keratinocytes might contain opiate receptors. In a series of experiments they demonstrated that human epidermal keratinocytes expressed the mRNA and protein (detected by immunohistochemistry) for the μ-opiate receptor. Given the correlation between the locations of the mRNA and protein, they concluded that the μ-opiate receptor is both transcribed and functional. To demonstrate the latter point human skin cultures were incubated with naloxone or β-endorphin with subsequent downregulation of the μ-opiate receptor compared to control. An extension of this research (Bigliardi-Qi *et al*, 2000) provided data supporting the association of the μ-opiate receptor and β-endorphin in the pathogenesis of psoriasis.

Given that morphine has a greater affinity for the μ-opiate receptor than β-endorphin and the presence of these receptors in the epidermis, we investigated the interaction of endogenous morphine with this receptor, utilizing neonatal foreskin samples. A rabbit-derived polyclonal antimorphine antibody obtained from S. Spector (Oka *et al*, 1985) was used in this study. This antibody did not recognize any of the opioid peptides (enkephalins, endorphins, dynorphins, and their fragments), did not bind to the narcotic antagonists naloxone or naltrexone (unpublished data), and was therefore considered specific for morphine. This antibody was used to detect immunoreactive morphine in the foreskin samples. The results indicated a selective localization of ligand in the epidermis, more pronounced in the basal layer (**Fig 1**). These preliminary results suggest that endogenous morphine is a functionally active physiologic ligand for the μ-opiate keratinocyte receptor in human skin.

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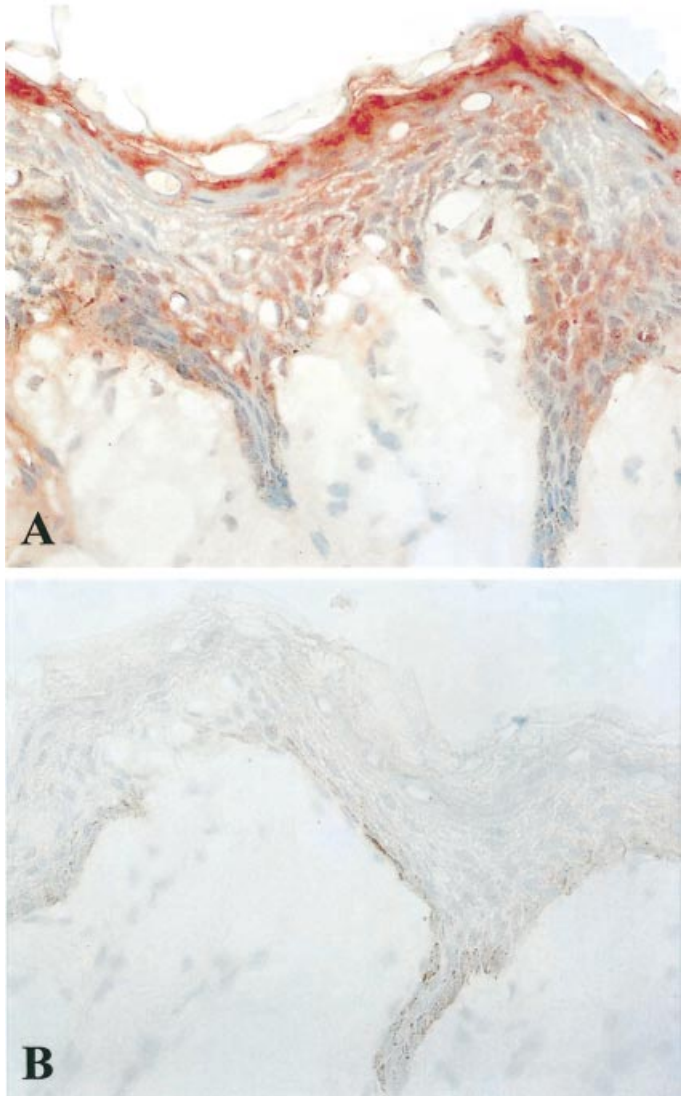

Figure 1. Immunoperoxidase staining of neonatal foreskin with antimorphine antibody. (*A*) Presence of primary antibody; (*B*) absence of primary antibody. Magnification 40×.

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